Please cancel claims 20-23.

Claims 24-26, previously found free of the prior art (in paragraph 8 of the June 2, 1999 Office Action), remain under consideration in this application. Below the limitations of the related independent claim 20, and intervening dependent claims, are added to claims 24-26, to place them in condition for allowance.

A marked-up version of claims 24-26 is provided in a separate paper.

Claim 24 has been amended as follows:

24. (Amended) A method of identifying ligands that modulate a *Drosophila* membrane sodium channel, which comprises:

(a) expressing an isolated *Drosophila para* voltage-activated sodium channel, and expressing an isolated *Drosophila* voltage activated putative beta subunit *tipE* in a *Xenopus* oocytes host cell, wherein said expressing of *para* and *tipE* occurs after coinjection of *para* and *tipE* RNA, wherein said *para* RNA is encoded by the DNA molecule as set forth in SEQ ID NO: 7, wherein the sodium channel is tetrodotoxin sensitive, and wherein the host cell expresses a voltage-activated sodium current;

(b) contacting the host cell with a ligand;

(c) measuring the resulting voltage-activated current; and

(d) comparing the voltage-activated current measured according to step (c) with voltage-activated current measured upon contacting said ligand with a control host cell in which said *para* and said *tipE* are not co-expressed.

Claim 25 has been amended as follows:

25. (Amended) A method of identifying ligands that modulate a *Drosophila* membrane sodium channel, which comprises:

(a) co-expressing an isolated *Drosophila para* voltage-activated sodium channel and an isolated *Drosophila* voltage activated putative beta subunit, *tipE*, in a host cell from a multicellular organism, wherein said expressing of *para* and *tipE* occurs after an isolated DNA molecule encoding *para* and an isolated DNA molecule encoding *tipE* are introduced into said host cell, wherein said isolated DNA molecule which expresses *para* is as set forth in SEQ ID NO: 7, wherein the sodium channel is tetrodotoxin sensitive, and wherein the host cell expresses a voltage-activated sodium current;

(b) contacting the host cell with a ligand;

(c) measuring the resulting voltage-activated current; and

(d) comparing the voltage-activated current measured according to step (c) with voltage-activated current measured upon contacting said ligand with a control host cell in which said *para* and said *tipE* are not co-expressed.

Claim 26 has been amended as follows:

26. (Amended) A method of identifying ligands that modulate a *Drosophila* membrane sodium channel, which comprises:

(a) expressing an isolated *Drosophila para* voltage-activated sodium channel, and expressing an isolated *Drosophila* voltage activated putative beta subunit *tipE* in a host cell selected from the group consisting of

Xenopus oocytes and a cell from a multicellular organism, wherein an isolated DNA molecule which expresses *para* comprises a DNA sequence as set forth in SEQ ID NO: 7, wherein the sodium channel is tetrodotoxin sensitive, and wherein the host cell expresses a voltage-activated sodium current;

(b) contacting the host cell with a ligand;

E' f1

(c) measuring the resulting voltage-activated current;

(d) comparing the voltage-activated current measured according to step (c) with voltage-activated current measured upon contacting said ligand with a control host cell in which said *para* and said *tipE* are not co-expressed and

(e) comparing the voltage-activated current measured according to step (c) with voltage-activated current produced prior to contacting the host cell with the ligand.

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4. Regarding paragraph 4 of the 07/12/02 Office Action, which refers to a 35 U.S.C. 112, second paragraph rejection in a previous Office Action, Applicant has addressed the first issue by adding the limitation "wherein the sodium channel is tetrodotoxin sensitive" to each of claims 24 to 26. As to the second issue, the period after the term "tipE" has already been corrected in a previous Response, and there is no period after such term in the present claims.

5. Regarding paragraph 5 of the 07/12/02 Office Action, which refers to a 35 U.S.C. 112, first paragraph rejection in a previous Office Action, Applicant has addressed this rejection as follows. First, Applicant has amended part "(d)" of the above claims by replacing the final words ". . . in which said *para* and said *tipE* are not co-expressed." with "which is not treated with said ligand."

Support for such amendment is as follows. Page 17, lines 3 to 23, generally describe different approaches to assaying receptor modulators. Various

types of modulators are described (e.g., see last sentence of the paragraph), and it is disclosed that evaluations of candidate modulators may be conducted with or without the presence of a "known labelled (sic) or unlabelled (sic) sodium channel modulator." (See lines 15-16.)

More specifically, at the end of Example 5, on page 33, lines 15-21, state:

> Cells that are expressing *para* and *tipE*, stably or transiently, are used to test for expression of voltage-activated sodium channels and for ligand binding activity. These cells are used to identify and examine other compounds for their ability to modulate, inhibit, or activate the *para* voltage-activated sodium channel as described herein. (Underline emphasis added.)

Example 9, starting on page 35, line 26, describes and cites references to specific methods that are used for testing ligands. This supports the above paragraph, and represents part of what is "described herein." In particular, but without being limiting, three sentences starting on page 36, line 8 read,

> To identify sodium channel agonists, *para* transfected cells are aliquoted into each well of a 96-well microtiter dish and [22Na] is added to the culture media, test compounds are added to each well and agonists are identified by an increase in [22Na] uptake as compared to untreated cells. Specificity is determined by blocking [22Na] uptake with tetrodotoxin. Likewise, sodium channel antagonist can be identified by screening for compounds that block [22Na] uptake following activation of the *para* voltage-activated sodium channel. (Underline emphasis added.)

Other sections of Example 9 are rightfully applicable to cells that are expressing *para* and *tipE* based on the "as described herein" reference underlined above.

Also, and in thc alternative, it should be recognized Example 9 should be understood to refer to cells having channels formed as a result of the coinjection of *para* and *tipE* DNA or RNA. This is supported by the statement elsewhere in the specification, that "[w]hen coexpressed in

Xenopus ooctyes *para* and *tipE* encode proteins that produce a voltage-activated sodium channel that is blocked by tetrodotoxin." (Page 16, lines 26-30) Later, in the next paragraph, it is stated "In general, an assay procedure to identify insect sodium channel modulators will contain the *para* voltage-activated sodium channel of the present invention, and a test compound which contains a putative sodium channel modulator." (Page 17, lines 6-9) It is believed that referring to a "*para* voltage-activated sodium channel" in Example 9, and elsewhere, is merely a 'shorthand convention' for the present invention in which both *para* and *tipE* are cointroduced to a cell, and thereafter encode proteins that produce a voltage-activated sodium channel that comprises *para* protein.

6. A Supplemental Information Disclosure Statement (IDS) is provided herewith. Applicant notes that the patent provided in this Supplemental IDS (U.S. 5,871,940) is from a divisional application of the Hall et al. patent that was a basis for rejection of claims 20-23 (see paragraph 7 of Final Office Action). Accordingly, it is believed that the newly provided reference does not impact the patentability of claims 24-26 presented for allowance herein.

7. The Applicant believes the claims as amended are in condition for allowance. Should the Examiner view the claims otherwise, a telephone call to the Attorney for Applicant will be appreciated.

Respectfully Submitted,

By _____
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Attorney/Agent for Applicant(s)
Reg. No.: 51210

Date: November 12, 2002

Telephone No.: 407-240-0085

I hereby certify that this correspondence is being forwarded via Facsimile No. 703-305-7939 to ATTN: Examiner Patrick Nolan, Commissioner for Patents, Washington, D.C. 20231.

Date of Deposit: November 12, 2002

Typed Name: Joseph Fischer

Signature: _____